## REMARKS/ARGUMENTS

### I. Status of the Claims

Claims 47, 49-52, and 54-56 are pending.

### II. Claim Rejections

A. 35 U.S.C. §101

Claims 47, 50-52, and 54-56 were rejected under 35 U.S.C. §101 for alleged lack of a specific and substantial asserted utility or a well established utility. Applicants respectfully traverse the rejection.

The present application specifically asserts Slo3's role in sperm physiology and its use for identifying modulators of the ion channel, which can be used for treating fertility related conditions. The Examiner appeared to believe, however, that the asserted utility is "speculative" and can only be ascertained through "further research" (pages 3-5, particularly page 5 lines 8-13 of the March 11, 2003, Office Action). Citing the Schreiber reference (attached as Exhibit A with the preliminary amendment Applicants filed on February 10, 2003) and Dr. Jegla's declaration, the Examiner placed much emphasis on the "may be" and "could be" type of language used in the two documents and concluded that the asserted involvement of Slo3 in sperm capacitation and acrosome reaction is unproven because "there is no showing in the specification or prior art to conclude such a statement" (page 5 lines 8-13 of the Action). Applicants respectfully note that the Examiner's position is inconsistent with the utility standard set forth both in the MPEP and prevailing case law.

*1. Standard to Assess Utility*

According to MPEP §2107, the Examiner should review the claims and the supporting written description to determine whether the utility requirement under 35 U.S.C. §101 is met. No rejection based on lack of utility should be made if an invention has a well-established utility, *i.e.*, a utility that will be immediately appreciated by one of ordinary skill in the art based on the characteristics of the invention, regardless any such utility has been asserted.

Neither should any rejection be made for lack of utility if an applicant has asserted a specific and substantial utility that would be considered credible by one of ordinary skill in the art.

In most cases, an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101. MPEP §2107.02 III A. The Court of Customs and Patent Appeals stated in *In re Langer*:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of §101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

*In re Langer*, 183 USPQ 288, at 297 (CCPA, 1974, emphasis in original). To overcome the presumption of sufficient utility as asserted by an applicant, the Examiner must carry the initial burden to make a *prima facie* showing of lack of utility and provide a sufficient evidentiary basis for the conclusion. In other words, the Examiner "must do more than merely question operability--[he] must set forth factual reasons which would lead one skilled in the art to question objective truth of the statement of operability." *In re Gaubert*, 187 USPQ 664, 666 (CCPA 1975).

MPEP §2107.02 IV further states, a detailed explanation should be given for a utility rejection as to why the claimed invention has no specific and substantial asserted utility. Documentary evidence should be provided when possible. Otherwise the Examiner should specifically explain the scientific basis for his factual conclusions.

**2. The Asserted Utility Is Specific and Substantial**

The present specification provides, for the first time, the isolated polynucleotide and amino acid sequences for Slo3, a pH sensitive, voltage-gated potassium channel expressed in spermatocytes. Pending claims are directed to Slo3 potassium channel and its variants. In describing the physiological role of the potassium channels, the specification states, "Slo3 is involved in sperm capacitation and/or the acrosome reaction, essential steps in fertilization" (page 9 lines 28-29 of the specification). Furthermore, the present application specifically

asserts the utility of the claimed Slo3 channels. For instance, the Slo3 channels "are useful for testing inhibitors or activators of Slo3," which "can be used therapeutically to treat infertility conditions related to sperm physiology, or as contraceptives" (*see, e.g.*, page 12 line 24 and lines 26-27 of the specification).

Applicants contend that the present invention has a specific utility. Specific utility is defined by the MPEP as a utility that is specific to the subject matter claimed. The MPEP explains that applications show sufficient specific utility when applicants disclose a "specific biological activity" and reasonably correlate that activity to a "disease condition." MPEP §§2107.01 and 2107.02. In the present application, Applicants disclose a "disease condition," *e.g.*, infertility, that correlates with a "biological activity," *i.e.*, the opening and closing of Slo3 potassium channels. This asserted utility is specific for the claimed Slo3 potassium channels and not just any ion channels.

Applicants also contend that the present invention has a substantial utility or a "real-world" use. The specification states that compounds capable of modulating Slo3 potassium channels are useful for treating infertility conditions or can be used as means of contraceptives. *See, e.g.*, last paragraph on page 12. This asserted utility is a "real-world" use.

***3. The Examiner Has Not Established A Prima Facie Showing of Lack of Utility***

The Examiner rejected pending claims for alleged lack of utility, alleging that the asserted utility is speculative and undetermined. Specifically, the Examiner reached this conclusion because both the Schreiber reference and Dr. Jegla's declaration stated that Slo3 "may be" or "could be involved in," instead of "is required for," sperm capacitaion and acrosome reaction (page 5 lines 8-13 of the March 11, 2003, Office Action). In other words, the Examiner was doubtful of the specific and substantial utility asserted by Applicants.

Raising a rejection for lack of utility in such a manner is inconsistent with the proper practice described in the MPEP, which places the initial burden on the Examiner, not Applicants, to provide evidence to support a factual conclusion of the credibility of an asserted utility. In fact, MPEP §2107.02 III.B. specifically cautions Office personnel that, once an

assertion of a particular utility is made, "that assertion cannot simply be dismissed ..... as 'wrong,' even when there may be reason to believe the assertion is not entirely accurate." Instead, the Examiner must provide an explanation setting forth the reasoning used in concluding that the asserted specific and substantial utility is not credible; support for factual findings relied upon in reaching the conclusion; and an evaluation of all relevant evidence of record, including utilities taught in the closest prior art. MPEP §2107.02 IV.

In the instant case, the Examiner has provided none of the above. Even the Schreiber reference, which the Examiner cited to show that Slo3's function is unknown in sperm physiology, does not say that Slo3 is not involved in such process. Contrary to the Examiner's interpretation, the reference in fact supports Slo3's functional role as asserted by Applicants (See Abstract of the Schreiber reference, "Slo3 could be involved in sperm capacitation and/or the acrosome reaction"), only not in absolute terms. According to the MPEP, this reference cannot serve as a valid evidentiary basis for the Examiner to overcome the presumption of sufficient utility. As such, Applicants respectfully submit that a *prima facie* showing of lack of utility is not established and the rejection thus cannot properly stand.

B. 35 U.S.C. §112 First Paragraph

Claims 47, 50-52, and 54-56 were further rejected under 35 U.S.C. §112 first paragraph for alleged inadequate enablement. Applicants respectfully traverse the rejection.

The Examiner stated that since the present invention does not have a specific and substantial utility, one of skill in the art would not know how to use the claimed invention. As discussed above, the claimed invention does have a specific and substantial utility. Thus, Applicants respectfully request that the enablement rejection on this ground be withdrawn.

The Examiner also alleged inadequate enablement because "Applicant has not disclosed how to use the variant channel proteins which may have unit conductance of 80-120 pS, some structural similarity to Slo3 of SEQ ID NO:16, but be functionally different." Applicants cannot agree with this reasoning. Pending claims are drawn to polypeptide monomers of a pH sensitive potassium channel, each of the monomers (i) forms a potassium

channel having a unit conductance of 80-120 pS and having increased potassium channel current amplitude above intracellular pH of 7.1, when the monomer is expressed in Xenopus oocyte; and (ii) is encoded by a nucleic acid that specifically binds under stringent hybridization conditions to the complement of a nucleic acid encoding an amino acid sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:16 or SEQ ID NO:18, wherein the hybridization reaction is incubated at 42°C in a buffer comprising 50% formamide, 5x SSC, and 1% SDS, and washed at 65°C in a buffer comprising 0.2x SSC and 0.1% SDS. In other words, claimed potassium channel monomers have commonly shared functional features as defined in (i)--having a unit conductance of 80-120 pS and increased current amplitude above intracellular pH of 7.1. Those functionally different yet structurally similar polypeptides are thus not encompassed by the claim scope. Moreover, the specification teaches assays that can be used to test a candidate polypeptide for the defined functional features in terms of unit conductance and current amplitude, *see, e.g.*, Example IV from page 60 line 5 to page 61 lines 29. Using these assays, one ordinarily skilled in the art could easily determine if a particular polypeptide is within the claimed genus of polypeptides, based on its functionality in terms of unit conductance and current amplitude, and thus exclude inoperable embodiments.

If by "functionally different," the Examiner was referring to different physiological functions the claimed polypeptides may have, Applicants note that there is no evidence suggesting diverse physiological functions among the claimed polypeptides. Applicants made the assertion of utility based on the fact that the human and mouse versions of Slo3 (hSlo3 and mSlo3) are recognized as orthologs with identical physiological functions. In the Schrieber et al. reference, submitted as Exhibit A along with the communication filed by Applicants on February 10, 2003, two of the present inventors describe the cloning and expression of mSlo3. The mSlo3 nucleotide sequence is provided as Figure 1 of the Schrieber reference and SEQ ID NO:2 of the present application. Structurally, the full length nucleotide sequence of mSlo3 (SEQ ID NO:2) encodes a protein of 1113 amino acids (SEQ ID NO:1) with a predicted molecular mass of 126 kDa. The authors also indicate that a homolog hSlo3 is present human testis. The hSlo3 nucleotide sequence is described in SEQ ID NOs:17 and 19 of

the present application, and the amino acid sequence of hSlo3 is provided by SEQ ID NOs:16 and 18. As described in the specification on pages 62-63, the hSlo3 sequences were cloned from a human testis cDNA library using PCR primers based on the mSlo3 sequence. The hSlo3 nucleotide sequence thus obtained was determined by the inventors of the present application to be highly homologous to the mSlo3 sequence, with high identity in the S1 region (part of the core domain). The specification describes that hSlo3 encodes a protein of similar size, sequence identity, and expression pattern as its mouse homologue (*see* Example 2 of the specification, in particular page 62 line 21 to page 63 line 2). Northern blot analysis showed that hSlo3 was specifically expressed in the human testis (page 63 lines 1-2) with high sequence homology to mSlo3. As hSlo3 is recognized as the counterpart or ortholog of mSlo3, one of skill in the art would accept that polypeptides encoded by the two sequences have the same physiological functions. Without any evidence that a class of polypeptides sharing a high level of structural and functional similarity as specifically defined by the claims would have distinctly different physiological functions, Applicants submit that it would be inappropriate to require Applicants to provide utility for such imaginary functions.

The Examiner further alleged that the claimed invention is not fully enabled, citing large quantity of experimentation necessary to identify polypeptides encompassed by claims reciting hybridization, insufficient guidance provided by the specification, and unpredictability of the effects of mutations on the structure and function of a polypeptide. Applicants respectfully disagree.

A claimed invention is enabled when the disclosure allows one of ordinary skill in the art to make and use the invention without undue experimentation. MPEP §2164.01. The test for enablement as set forth in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), requires the consideration of multiple factors: the breadth of the claims; the nature of the invention; the state of the prior art; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In the present case, the claims are directed to polypeptide monomers of a pH sensitive potassium channels with well-defined structures and readily testable functional features. The specification contains ample directions to practice the invention, such as methods of cloning pH sensitive potassium channel coding sequences (*see, e.g.*, page 29 line 1 to page 32 line 9), expression of the ion channels (*see, e.g.*, page 32 line 12 to page 34 line 21), purification of the expressed ion channels (*see, e.g.*, page 34 line 24 to page 37 line 22), production of antibodies against the claimed ion channels (*see, e.g.*, page 37 line 32 to page 39 line 18), immunological detection of the claimed ion channels (*see, e.g.*, page 39 line 21 to page 44 line 8), assays for compounds that increase or decrease ion flux (*see, e.g.*, page 44 line 11 to page 48 line 20), and cellular transfection of the ion channels (*see, e.g.*, page 48 line 23 to page 52 line 12). The level of technical sophistication is high in the art, and the pH sensitive potassium channel variants can be readily tested according to the methods commonly used by those skilled in the art or the methods taught by the specification (such as nucleic acid or amino acid sequence comparison, nucleic acid hybridization assays, and assays for ion channels with the defined pH sensitive characteristics) to eliminate inoperable embodiments. Working examples are also provided in the instant specification. MPEP §2164.01 states, complex experimentation is not necessarily undue, if the art typically engages in such experimentation. In the present case, although some experimentation may be involved to practice the claimed invention using embodiments other than those specifically described in the application, such experimentation utilizes well-established techniques and is the type routinely conducted in the art. Thus, the experimentation does not constitute undue experimentation.

Taken together, analysis of the *Wands* factors indicates proper enablement of the claimed invention. Applicants thus respectfully request the withdrawal of the enablement rejection.

## CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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